CLAIMS

1. *In vitro* method of documenting a repertoire of (an) NKR immunoreceptor(s) comprising in particular the KIR p58.1, p58.2, p70.INH and p140.INH, and the NKG2A and NKG2B receptors, and/or of a repertoire of (an) NKR immunoreceptor counterpart(s), comprising in particular the KAR p50.1, p50.2, p70.ACT and p140.ACT receptors, and the NKG2C, NKG2D, NKG2E and NKG2F receptors, these immunoreceptors being designated hereinafter target receptor(s), characterized in that it comprises:

i. the use of at least one pair of oligonucleotides, one being designated 3′ oligonucleotide and the other 5′ oligonucleotide, the 3′ and 5′ oligonucleotides of the same said pair both being capable, under hybridization conditions corresponding to incubation for 1 min in a buffer [20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM $MgCl_2$] at a temperature of between 50°C and 65°C approximately, of hybridizing to the DNA or to the cDNA of a target NKR receptor, or NKR counterpart, but not hybridizing, under the same hybridization conditions, with the DNA or the cDNA of an NKR receptor counterpart, or respectively of an NKR receptor, functional counterpart of the said target receptor,

ii. the bringing of DNA or cDNA populations of a biological sample of human or animal origin for which it is desired to document the repertoire of (a) target immunoreceptor(s), into contact with an excess of at least one 3′ and 5′ oligonucleotide pair according to i. under conditions favourable to the hybridization of this 3′ and 5′ oligonucleotide pair with the DNAs or cDNAs of the biological sample, and

iii. the detection of the possible hybrids formed between these DNAs or cDNAs and the 3′ and 5′ oligonucleotide pair(s).

2. Method according to Claim 1, characterized in that the said or at least one of the said 3′ and 5′ oligonucleotide pair(s) used is in addition capable,

under the same hybridization conditions as those defined under i., of not hybridizing to the DNA or cDNA of a receptor, either NKR or NKR counterpart, other than the said target receptor.

3. Method according to any one of the preceding claims, characterized in that the 5′ oligonucleotide of a said 3′ and 5′ oligonucleotide pair used for an NKR target receptor (or NKR counterpart) is capable, under the same said hybridization conditions, of hybridizing to the DNA or to the cDNA of an NKR receptor counterpart (or respectively NKR receptor), functional counterpart of the said NKR target receptor (or respectively NKR receptor counterpart).

4. Method according to any one of the preceding claims, characterized in that the 3′ oligonucleotide of a said 3′ and 5′ oligonucleotide pair, used for a KAR target receptor, is capable, under the same said hybridization conditions, of hybridizing to the DNA or cDNA of the said KAR target receptor at the level of a nucleotide stretch which comprises a sequence corresponding, according to the universal genetic code, and taking into account the degeneracy of the said code, to the amino acid sequence Lys Ile Pro Phe Thr Ile (K I P F T I) or Lys Leu Pro Phe Thr Ile (K L P F T I) (SEQ ID No. 26 or 27).

5. Method according to any one of the preceding claims, characterized in that the said (or at least one of the said) 3′ and 5′ oligonucleotide pair(s) having as target receptor a KIR receptor is chosen from the group of 3′ and 5′ oligonucleotide pairs consisting of:
a 5′ oligonucleotide comprising the sequence SEQ ID No. 1, or a sequence which is derived therefrom, and at least one 3′ oligonucleotide comprising the sequence SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom,
a 5′ oligonucleotide comprising the sequence SEQ ID No. 4, or a sequence which is derived therefrom, and at least one 3′ oligonucleotide comprising the sequence

SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom,

a 5′ oligonucleotide comprising the sequence SEQ ID No. 9, or a sequence which is derived therefrom, and at least one 3′ oligonucleotide comprising the sequence SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom,

at least one 5′ oligonucleotide comprising the sequence SEQ ID No. 10, No. 11, No. 12 or No. 13, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 14, or a sequence which is derived therefrom.

6. Method according to any one of the preceding claims, characterized in that the said (or at least one of the said) 3′ and 5′ oligonucleotide pair(s) having as target receptor a KAR receptor is chosen from the group of 3′ and 5′ oligonucleotide pairs consisting of:

- a 5′ oligonucleotide comprising the sequence SEQ ID No. 1, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 3, or a sequence which is derived therefrom,
- a 5′ oligonucleotide comprising the sequence SEQ ID No. 8, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 3, or a sequence which is derived therefrom,
- a 5′ oligonucleotide comprising the sequence SEQ ID No. 9, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 3, or a sequence which is derived therefrom,
- a 5′ oligonucleotide comprising the sequence SEQ ID No. 15, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 3, or a sequence which is derived therefrom.

7. Method according to any one of the preceding claims, characterized in that the said (or at least one of the said) 3′ and 5′ oligonucleotide pair(s) having as target receptor a NKG2 receptor is chosen from the group of 3′ and 5′ oligonucleotide pairs consisting of:

a 5′ oligonucleotide comprising the sequence SEQ ID No. 16, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 17, or a sequence which is derived therefrom,

a 5′ oligonucleotide comprising the sequence SEQ ID No. 18, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 17, or a sequence which is derived therefrom,

a 5′ oligonucleotide comprising the sequence SEQ ID No. 19, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 17, or a sequence which is derived therefrom,

a 5′ oligonucleotide comprising the sequence SEQ ID No. 20, or a sequence which is derived therefrom, and a 3′ oligonucleotide comprising the sequence SEQ ID No. 21, or a sequence which is derived therefrom.

8. Method according to any one of the preceding claims, characterized in that the two 3′ or 5′ oligonucleotides of the same said pair are each coupled to a marker, in particular coupled to a fluorescent or radioactive marker, such as ^{32}P, allowing the visualization of the hybrids which they may form with the said DNA or cDNA populations of the said biological sample.

9. Method according to any one of the preceding claims, characterized in that the said 3′ and 5′ oligonucleotide pair(s) serve(s) as 3′ and 5′ primers, respectively, for extension by DNA polymerase.

10. Method according to any one of the preceding claims, characterized in that the said hybrids which may be formed are amplified by at least one PCR prior to their detection.

11. Method according to any one of the preceding claims, characterized in that the said hybrids which may be formed are amplified by nested PCR.

12. Method according to any one of the preceding claims, characterized in that the said detection of the hybrids which may be formed comprises, in addition, the

resolution, on a polyacrylamide gel, of the reaction mixture derived from the bringing into contact, as well as the visualization of the presence or of the absence of electrophoretic bands containing the said hybrids which may be formed.

13. Method according to any one of the preceding claims, characterized in that it is applied to the documentation of a genotypic repertoire of NKR immunoreceptors and/or of NKR immunoreceptor counterparts.

14. Method according to any one of the preceding claims, characterized in that it is applied to the documentation of an expression repertoire of NKR immunoreceptors and/or of NKR immunoreceptor counterparts.

15. Method according to any one of the preceding claims, characterized in that the said biological sample of human or animal origin is peripheral blood, bone marrow, lymphocytes, NK and/or T cells, transgenic cells expressing immunoreceptors and a fraction isolated from these samples.

16. Method according to any one of the preceding claims, characterized in that it is applied to the screening of a library of organs, tissues or cells.

17. Method according to any one of the preceding claims, characterized in that it is applied to the prediction or to the monitoring of the acceptance or rejection, by a human or an animal, of cells, tissue or organ which is (are) genetically different.

18. Method according to any one of the preceding claims, characterized in that it is applied to the prediction or to the monitoring of the safety or of the pathogenicity (GVH), for a human or an animal, of a graft or transplant, of cells, tissue or organ which is (are) genetically different.

19. Method according to any one of the preceding claims, characterized in that it is applied to the prediction or to the monitoring, for a human or an

animal, of a GVL-type effect on the part of cells, tissue or organ which is (are) genetically different.

20. Method according to any one of the preceding claims, characterized in that it is applied to the determination of the state of activation of NK and/or T cells at a given instant in an animal or a human.

21. Method according to any one of the preceding claims, characterized in that it is applied to the prediction or to the monitoring of the state of resistance of an animal or a human towards a viral infection, such as an HIV infection, or a parasitic infection, such as malaria, or a bacterial infection, towards an autoimmune disease, such as rheumatoid arthritis, or alternatively towards the development of malignant cells such as leukaemia cells.

22. Method according to any one of the preceding claims, characterized in that it is applied to the screening of medicaments which are active on infectious diseases, on autoimmune diseases and on tumour diseases.

23. Kit for carrying out the method according to any one of Claims 1 to 22, characterized in that it comprises, in a container, at least one said 3' and 5' oligonucleotide pair, the reagents for carrying out the said method(s) such as a buffer, a marker (optionally coupled to the oligonucleotides of the said pair), as well as instructions for use.